Express Mail No. EM016027553US

VOS-22 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Christian Plank, et al.
Application No.	:	10/023,317 Confirmation No.: 2272
Filed	:	December 17, 2001
For	:	COMBINATIONS FOR INTRODUCING NUCLEIC ACIDS INTO CELLS
Group Art Unit	:	1635
Examiner	:	Angell, Jon E.

New York, New York
June 22, 2007

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

DECLARATION OF CHRISTIAN PLANK UNDER 37 C.F.R. § 1.132

I, Christian Plank, a citizen of Austria, residing at Ulrich-Haid-Strasse 1, 82229, Seefeld, Germany, hereby declare and state as follows:

1. I am one of the co-inventors of the subject matter described and claimed in the above-identified application.

2. I am currently a research group leader at the Institute of Experimental Oncology and Therapy Research, Technical University, München, Germany. I have held this position since 1997.

3. For the past 17 years, I have studied synthetic constructs for nucleic acid delivery into cells including every step from chemical synthesis, gene vector assembly and biophysics to use of such constructs for nucleic acid delivery in cell cultures and in vivo.

I have attached my curriculum vitae (Exhibit A), which lists my educational background and professional activities. It also lists the articles that I have authored or co-authored and published in peer-reviewed scientific journals and at seminars at various scientific meetings.

4. I have read and am familiar with the February 22, 2007 Office Action in the above-identified application. I understand that, in the Examiner's view, the specification is only enabling for PEI/nucleic acid-P3YE5C, Polylysine/nucleic acid P3INF7, DOTAPcholesterol/nucleic acid-P3YE5C, DOTAP/cholesterol/nucleic acid-P6YE5C, and PEI/nucleic acid-P6YE5C.

5. I make this declaration to demonstrate that a person of ordinary skill in the art, following the teachings of the specification, would be able to obtain the claimed compositions and practice the claimed methods without undue experimentation.

6. Exhibit B depicts the results of experiments carried out by me and/or under my direction. The results demonstrate that two co-polymer formulations—formulations that are not specifically exemplified in the specification of the above-identified application, as filed, but that fall under the definition of Formula I—are able to form complexes with DNA and deliver the DNA into HeLa cells.

7. In the experiments, the cationic peptide SV404 $(PKKKRKVG)_4C$ was synthesized according to the FastMoc™ protocol using an Applied Biosystems® 431A peptide synthesizer. The peptide was purified by reverse phase chromatography, lyophilized and redissolved in deionized water. The peptide was coupled to the intermediates 3 or 4 (see Fig. 1 of the above-identified application) via disulfide bridge formation in complete analogy to what is described in the specification for the peptide $(YEEEEE)_2K$-ahx-C (see Fig. 2 of the above-identified application and paragraphs [0146]-[0153] of the published application). The products, designated P6-SV404 and P3-SV404 respectively, were purified by size exclusion chromatography on a Sephadex® 75 size exclusion column with 20 mM HEPES pH 7.4 / 3 M sodium chloride as elution buffer. The product fractions were dialyzed against 20 mM HEPES pH 7.4. The concentrations of the polymers (and at the same time of the coupled peptides) were determined by a ninhydrin assay using the HPLC-purified peptide SV404 as a

calibration standard. Plasmid DNA binding and compaction were determined by dynamic light scattering measurements (Malvern Zetasizer™ 3000HS) as well as by fluorescence quenching measurements using the DNA intercalating dye PicoGreen® (Molecular Probes®). These measurements demonstrated that the copolymers P6-SV404 and P3-SV404 bind and compact DNA.

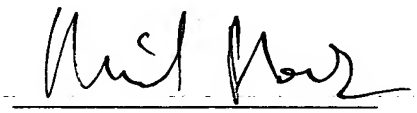
DNA binding and compaction were also determined in the presence of the endosomolytic peptide INF7, which is described in the specification. For this purpose, the peptide INF7 was fluorescence-labeled with fluorescein, the fluorescence of which is quenched when compacted in a DNA complex by a polycation. Plasmid DNA was mixed at various ratios with the fluorescence-labeled peptide and then compacted by the addition of P6-SV404 and P3-SV404, respectively. The measurements demonstrated that P6-SV404 and P3-SV404 readily form DNA complexes comprising the endosomolytic peptide INF7.

In order to demonstrate the potency of P6-SV404 and P3-SV404 in gene delivery, a transfection experiment with the luciferase reporter gene was carried out in HeLa cells. The day prior transfection, 20,000 cells per well were seeded in 96-well plates. Two stock solutions in 20 mM HEPES pH 7.4 were prepared containing plasmid DNA (coding for luciferase under the control of the CMV promoter) and 3 or 1 charge equivalent INF7 (one charge equivalent corresponds to 606 μmol peptide per gram DNA). A dilution series of the copolymers P6-SV404 and P3-SV404, respectively, was prepared in 20 mM HEPES pH 7.4 in a 96-well plate such as to result in charge ratios (positive over negative) of 10, 6.67 and 4.44, 2.96, 1.98, respectively, upon addition of aliquots of the DNA-INF7 stocks. The resulting DNA complexes were serially diluted in 20 mM HEPES pH 7.4 as well in order to derive a dose-response profile in gene delivery. Finally, the dilutions were adjusted to a final glucose concentration of 5 % by addition of a 50 % glucose stock solution. Aliquots of the resulting preparations (50 μl each) were transferred to the cells in triplicates so as to result in DNA doses of 500, 250, 125 and 62.5 ng per well. After 24 h of incubation, the luciferase assay was carried out, as described in the specification. The results demonstrated that both polymers are suitable to mediate gene delivery to cultured cells.

8. The products P6-SV404 and P3-SV404 referred to above and in Exhibit B fall under the general Formula I. In contrast to the polymer products exemplified in the specification (see, e.g., Figures 2 and 3 in the application), P6-SV404 and P3-SV404 are positively charged polymers. These above data demonstrate that charged copolymers of the general Formula I with entirely divergent chemical and physical properties fulfill their intended task in nucleic acid delivery.

9. Based on the teachings of the specification, which are confirmed by the data provided herein, a person of ordinary skill in the art would conclude that copolymers falling under the general Formula I are suitable for nucleic acid delivery into cells.

10. I declare further that all statements made herein of my own knowledge are true and that all statements made herein on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18, United States Code, and that such willful false statements may jeopardize the validity of this application and any patent issuing thereon.



Christian Plank

Signed at Munich, Germany
this 12 day of June, 2007.

 EXHIBIT A

Curriculum Vitae

Priv. Doz. Dr. rer.nat. Christian Plank

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Klinikum rechts der Isar der TU München
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Date and place of birth: September 3rd, 1963, Wels, Austria
Citizenship: Austrian
Marital Status: married

PROFESSIONAL EXPERIENCE

- ***3/1997-present:*** **Technische Universität München, Institute of Experimental Oncology**
Group leader – artificial virus-like delivery systems for nucleic acids and active agents. Deputy director of the institute. Development of nonviral gene vectors for gene therapy applications. Development of the Magnetofection™ technology (magnetically controlled and targeted nucleic acid delivery). Application of Magnetofection™ in immuno gene therapy of cancer (feline fibrosarcoma) in a veterinary clinical study. Development of magnetic microbubbles as carriers for active agents in drug delivery and in medical imaging. Development of polymers for the shielding and stabilization of nanoparticles ("*Protective Copolymers*"). Development of implantable carrier materials of nucleic acid vectors for tissue engineering, wound, cartilage and bone healing.

- ***11/2003***: **Foundation of OZ Biosciences S.A.R.L., Marseille, France.** This company was founded together with Olivier Zelphati and Jean Haensler, previous colleagues at the University of California in San Francisco. OZ Biosciences develops and markets reagents and technologies for the delivery of active substances to living cells. It caters to the international research community. OZ Biosciences reached it's break-even already in the second year of its existence. See www.ozbiosciences.com.

- ***3/1994-1/1997***: **University of California-San Francisco, CA, USA.**
Postdoctoral Fellow in the laboratory of Prof. Francis C. Szoka Jr., Department of Pharmacy and Biopharmaceutical Sciences. Development of gene delivery systems based on peptides. Biophysical studies for vector characterization. Characterization of the interaction of gene vectors with blood components.

HIGHER EDUCATION AND ACADEMIC DEGREES

2003-2004 **Habilitation** Technische Universität München, Medical Faculty. 2003 submission of the Habilitation thesis with the title „Synthetic nanoconstructs for gene delivery – from design to application". Degree of „Privatdozent" and venia legendi in 2004.

1990-1994 **University of Vienna, Vienna, Austria.**
Ph.D. degree (Dr. rer.nat.) in biochemistry, summa cum laude. Title of Ph.D. thesis: "Development of a Synthetic Virus-Like Gene Transfer System". Experimental work for the thesis carried out at the Research Institute of Molecular Pathology (I.M.P.), Vienna, Austria, in the laboratory of Prof. Ernst Wagner, part of the larger research team of Prof. Max L. Birnstiel.

1989-1990 **Research Institute of Molecular Pathology (I.M.P.), Vienna.**
Diploma thesis "Synthesis and application of biologically relevant peptides". Experimental work for the thesis carried out in the laboratory of Prof. Ernst Wagner.

1983 - 1990 **University of Vienna, Vienna, Austria. Diploma student in biochemistry.** Diploma (*Magister rerum naturalium)* in 1990, summa cum laude.

 EXHIBIT A

PRIMARY SCHOOL AND HIGH SCHOOL

1970-1974 Primary school (Volksschule) Braunau am Inn / Laab, Austria.

1974-1982 High School. Gymnasium Braunau am Inn. University entrance diploma (Abitur) 1982, summa cum laude. Grade point average 1,0.

HONOURS AND AWARDS

1994-1996. **Austrian Academy of Science.** Erwin Schrödinger Fellowship.

1996-1997. **Max Kade Foundation, New York and Austrian Academy of Science.** Max Kade Fellowship.

1998. **Award of the Federal Country of Upper Austria for Science („Talentförderungspreis Wissenschaft des Landes Oberösterreich").**

2001. **Best of Biotech Business Plan Competition**, Vienna. Award among the 10 best-ranked business plans.

2002. **Award of the Surgical Work Group Biomaterials of the German Surgical Society.**

SERVICE TO PROFESSIONAL PUBLICATIONS

Scientific reviewer for the journals Gene Therapy, Human Gene Therapy, Journal of Gene Medicine, Molecular Therapy, Journal of Vascular Research, Journal of Magnetism and Magnetic Materials, Biomacromolecules, Bionjugate Chemistry, FEBS Journal, Peptides, SMALL, Journal of Controlled Release, Blood, Nucleic Acids Research, Nature Methods, Proceedings of the National Academy of Sciences of the USA and others.

EXHIBIT A

PUBLICATIONS INCLUDING REVIEWED AND PUBLISHED ABSTRACTS

1. Rudolph C, Sieverling N, Schillinger U, Lesina E, Plank C, Thunemann AF, Schonberger H, Rosenecker J. Thyroid hormone (T3)-modification of polyethyleneglycol (PEG)-polyethyleneimine (PEI) graft copolymers for improved gene delivery to hepatocytes. Biomaterials 2007;28(10):1900-11.

2. Mykhaylyk O, Vlaskou D, Tresilwised N, Pithayanukul P, Moller W, Plank C. Magnetic nanoparticle formulations for DNA and siRNA delivery. Journal of Magnetism and Magnetic Materials 2007;311:275-281.

3. Dames P, Ortiz A, Schillinger U, Lesina E, Plank C, Rosenecker J, Rudolph C. Aerosol gene delivery to the murine lung is mouse strain dependent. J Mol Med 2007;85(4):371-8.

4. Xenariou S, Griesenbach U, Ferrari S, Dean P, Scheule RK, Cheng SH, Geddes DM, Plank C, Alton EW. Using magnetic forces to enhance non-viral gene transfer to airway epithelium in vivo. Gene Ther 2006.

5. Vlaskou D, Mykhaylyk O, Giunta R, Neshkova I, Hellwig N, Kroetz F, Bergemann C, Plank C. Magnetic Microbubbles: New Carriers for Localized Gene and Drug Delivery. Molecular Therapy 2006;13(Supplement 1):S290.

6. Schmidt CM, Huth S, Mykhaylyk O, Plank C, Rudolph C, Rosenecker J. Efficient Downregulation of ENaC Activity by Synthetic siRNAs. Molecular Therapy 2006;13(Supplement 1):S267.

7. Schillinger U, Schwarz B, Kempf T, Jahnke A, Fischer C, Loecher A, Schlemmer S, Hirschberger J, Brill T, Koestlin R, Gaensbacher B, Plank C. Immuno Gene Therapy of Feline Fibrosarcoma Using Intratumoral Magnetofection or Gene-Activated Matrices for Gene Delivery - Preliminary Results of a Veterinary Clinical Study. Molecular Therapy 2006;13(Supplement 1):S105.

8. Hellwig N, Plank C, Vlaskou D, Sohn HY, Pohl U, Krotz F. Ultrasound-enhanced microbubble-magnetofection: A new approach for efficient targeted delivery of nucleotides in vivo. Journal of Vascular Research 2006;43(6):549-549.

9. Dames P, Ortiz A, Schillinger U, Lesina E, Plank C, Rosenecker J, Rudolph C. Aerosol gene delivery to the murine lung is mouse strain dependent. J Mol Med 2006.

10. Bridell H, Plank C, Gloe T, Sohn HY, Pohl U, Krotz F. SHP-2 as a regulator of endothelial angiogenic signalling. Journal of Vascular Research 2006;43(6):563-563.

11. Schillinger U, Brill T, Rudolph C, Huth S, Gersting S, Krotz F, Hirschberger J, Bergemann C, Plank C. Advances in magnetofection - magnetically guided nucleic acid delivery. Journal of Magnetism and Magnetic Materials 2005;293(1):501-508.

12. Rudolph C, Ortiz A, Schillinger U, Jauernig J, Plank C, Rosenecker J. Methodological optimization of polyethylenimine (PEI)-based gene delivery to the lungs of mice via aerosol application. Journal of Gene Medicine 2005;7(1):59-66.

13. Rudolph C, Schillinger U, Ortiz A, Plank C, Golas MM, Sander B, Stark H, Rosenecker J. Aerosolized nanogram quantities of plasmid DNA mediate highly efficient gene delivery to mouse airway epithelium. Molecular Therapy 2005;12(3):493-501.

14. Plank C, Vlaskou D, Schillinger U, Mykhaylyk O, Brill T, Rudolph C, Huth S, Krotz F, Hirschberger J, Bergemann C. Localized nucleic acid delivery using magnetic nanoparticles. European Cells and Materials 2005;10(Suppl. 5):8.

15. Plank C, Scherer F, Rudolph C. Localized Nucleic Acid Delivery: A Discussion of Selected Methods. In: Schleef M, editor. DNA Pharmaceuticals. Weinheim: Wiley-VCH Verlag GmbH & Co. KGaA; 2005. p. 55-116.

16. Parak WJ, Pellegrino T, Plank C. Labelling of cells with quantum dots. Nanotechnology 2005;16(2):R9-R25.

17. Kolk A, Pautke C, Haczek C, Deppe H, Neff A, Stemberger A, Plank C. Non-viral BMP-2 gene transfer--A novel vector release out of a pdlla-coating of metallic surfaces to enhance the bone-implant interface. International Journal of Oral and Maxillofacial Surgery. Abstract of the 17th International Conference on Oral & Maxillofacial Surgery 2005;34(Supplement 1):73.

18. Hellwig N, Plank C, Vlaskou D, Bridell H, Sohn HY, Pohl U, Krotz F. Ultrasound-enhanced microbubble-magnetofection: a new approach for targeted delivery of nucleotides in vivo. Journal of Vascular Research 2005;42:86-87.

19. Bridell H, Plank C, Gloe T, Hellwig N, Sohn HY, Pohl U, Krotz F. Shp-2 is involved in bFGF dependent endothelial cell proliferation and prevents apoptosis. Journal of Vascular Research 2005;42:71-71.

20. Xenariou S, Griesenbach U, Bowden R, Hillery E, Doherty A, Geddes D, Porteous D, Plank C, Alton E, Boyd AC. Magnetofection to enhance transfection efficiency of large genomic context vectors in vitro. Molecular Therapy 2004;9:S182-S182.

21. Xenariou S, Griesenbach U, Ferrari S, Dean P, Scheule R, Cheng S, Geddes D, Plank C, Alton E. Magnetofection to enhance airway gene transfer. Molecular Therapy 2004;9:S180-S180.

22. Ueblacker P, Wagner B, Kruger A, Vogt S, DeSantis G, Kennerknecht E, Brill T, Hillemanns M, Salzmann GM, Imhoff AB, Plank C, Gansbacher B, Martinek V. Inducible nonviral gene expression in the treatment of osteochondral defects. Osteoarthritis and Cartilage 2004;12(9):711-719.

23. Schillinger U, Wexel G, Hacker C, Kullmer M, Stemberger A, Plank C. Copolymer-protected vector mediated BMP-2 gene delivery to articular chondrocytes in a 3-dimensional injectable fibrin matrix for tissue engineering. Molecular Therapy 2004;9:S321-S321.

24. Schillinger U, Kjaergaard N, Wiedmann K, Loecher A, Schlemmer S, Schwarz B, Kempf T, Hirschberger J, Koestlin R, Plank C, Gansbacher B, Brill T. Immuno gene therapy of feline fibrosarcoma using intratumoral magnetofection for gene delivery - Preliminary results of a veterinary clinical study. Molecular Therapy 2004;9:S216-S216.

25. Rudolph C, Ortiz A, Schillinger U, Jauernig J, Plank C, Rosenecker J. Improvement of aerosol delivery of polyethylenimine (PEI)-based gene vectors to the lungs of mice. Molecular Therapy 2004;9:S194-S194.

26. Rudolph C, Ortiz A, Schillinger U, Plank C, Rosenecker J. In vivo-gene expression of aerosolized PEI gene vector complexes is solvent-dependent. Molecular Therapy 2004;9:S193-S194.

27. Rudolph C, Schillinger U, Ortiz A, Tabatt K, Plank C, Muller RH, Rosenecker J. Application of novel solid lipid nanoparticle (SLN)-gene vector formulations based on a dimeric HIV-1 TAT-peptide in vitro and in vivo. Pharmaceutical Research 2004;21(9):1662-1669.

28. Plank C, Schillinger U, Hacker C, Brill T, Rudolph C, Krotz F, Hirschberger J, Stemberger A, Gansbacher B. Localized nucleic acid delivery to living cells using nanobiotechnology approaches. In: Nanotechnology, 2004. 4th IEEE Conference on; 2004; 2004. p. 242-244.

29. Huth S, Lausier J, Gersting SW, Rudolph C, Plank C, Welsch U, Rosenecker J. Insights into the mechanism of magnetofection using PEI-based magnetofectins for gene transfer. Journal of Gene Medicine 2004;6(8):923-936.

30. Griesenbach U, Dean P, Marshall N, Liang HD, Xenariou S, Geddes DM, Blomley MJ, Plank C, Alton E. Magnetofection and ultrasound to increase "naked" DNA delivery to the myocardium. Molecular Therapy 2004;9:S358-S358.

31. Gersting SW, Schillinger U, Lausier J, Nicklaus P, Rudolph C, Plank C, Reinhardt D, Rosenecker J. Gene delivery to respiratory epithelial cells by magnetofection. Journal of Gene Medicine 2004;6(8):913-922.

32. Erbacher P, Bettinger T, Brion E, Coll JL, Plank C, Behr JP, Remy JS. Genuine DNA/polyethylenimine (PEI) complexes improve transfection properties and cell survival. Journal of Drug Targeting 2004;12(4):223-236.

33. Bridell H, Krotz F, Plank C, Gloe T, Sohn HY, Pohl U. Inhibition of Shp-2 prevents human endothelial cell proliferation by inducing apoptosis. Journal of Vascular Research 2004;41(5):454-454.

34. Rudolph C, Plank C, Lausier J, Schillinger U, Muller RH, Rosenecker J. Oligomers of the arginine-rich motif of the HIV-1 TAT protein are capable of transferring plasmid DNA into cells. Journal of Biological Chemistry 2003;278(13):11411-11418.

35. Ritter W, Plank C, Lausier J, Rudolph C, Zink D, Reinhardt D, Rosenecker J. A novel transfecting peptide comprising a tetrameric nuclear localization sequence. Journal of Molecular Medicine-Jmm 2003;81(11):708-717.

36. Plank C, Schillinger U, Scherer F, Bergemann C, Remy JS, Krotz F, Anton M, Lausier J, Rosenecker J. The magnetofection method: Using magnetic force to enhance gene delivery. Biological Chemistry 2003;384(5):737-747.

37. Plank C. Magnetofection: Enhancing and targeting gene delivery with lipid-DNA vectors by magnetic force. Journal of Liposome Research 2003;13(1):105-106.

38. Plank C, Scherer F, Schillinger U, Bergemann C, Anton M. Magnetofection: Enhancing and targeting gene delivery with superparamagnetic nanoparticles and magnetic fields. Journal of Liposome Research 2003;13(1):29-32.

39. Plank C, Anton M, Rudolph C, Rosenecker J, Krotz F. Enhancing and targeting nucleic acid delivery by magnetic force. Expert Opinion on Biological Therapy 2003;3(5):745-758.

40. Mempel M, Voelcker V, Kollisch G, Plank C, Rad R, Gerhard M, Schnopp C, Fraunberger P, Walli AK, Ring J, Abeck D, Ollert M. Toll-like receptor expression in human keratinocytes: Nuclear factor kappa B controlled gene activation by Staphylococcus aureus is toll-like receptor 2 but not toll-like receptor 4 or platelet activating factor receptor dependent. Journal of Investigative Dermatology 2003;121(6):1389-1396.

41. Krotz F, de Wit C, Sohn HY, Zahler S, Gloe T, Pohl U, Plank C. Magnetofection - A highly efficient tool for antisense oligonucleotide delivery in vitro and in vivo. Molecular Therapy 2003;7(5):700-710.

42. Krotz F, Sohn HY, Gloe T, Plank C, Pohl U. Magnetofection potentiates gene delivery to cultured endothelial cells. Journal of Vascular Research 2003;40(5):425-434.

43. Hacker C, Brandt S, Plank C, Stemberger A. Fibrin-a new tool for gene delivery. AnnHematol 2003;82(Suppl. 1):S33.

44. Scherer F, Anton M, Schillinger U, Henkel J, Bergemann C, Kruger A, Gansbacher B, Plank C. Magnetofection: enhancing and targeting gene delivery by magnetic force in vitro and in vivo. Gene Therapy 2002;9(2):102-109.

45. Scherer F, Schillinger U, Putz U, Stemberger A, Plank C. Nonviral vector loaded collagen sponges for sustained gene delivery in vitro and in vivo. Journal of Gene Medicine 2002;4(6):634-643.

46. Rudolph C, Schillinger U, Plank C, Gessner A, Nicklaus P, Muller RH, Rosenecker J. Nonviral gene delivery to the lung with copolymer-protected and transferrin-modified polyethylenimine. Biochimica Et Biophysica Acta-General Subjects 2002;1573(1):75-83.

47. Finsinger D, Remy JS, Erbacher P, Koch C, Plank C. Protective copolymers for nonviral gene vectors: synthesis, vector characterization and application in gene delivery. Gene Therapy 2000;7(14):1183-1192.

48. Rosenecker J, Plank C, Hauck RW, Ernst N, Schmalix WA, Reinhardt D. Influence of surfactant and bronchoalveolar lavage fluid (BALF) on gene transfer with non-viral delivery systems. American Journal of Respiratory and Critical Care Medicine 1999;159(3):A435-A435.

49. Plank C, Tang MX, Wolfe AR, Szoka FC. Branched cationic peptides for gene delivery: Role of type and number of cationic residues in formation and in vitro activity of DNA polyplexes. Human Gene Therapy 1999;10(2):319-332.

50. Ernst N, Ulrichskotter S, Schmalix WA, Radler J, Galneder R, Mayer E, Gersting S, Plank C, Reinhardt D, Rosenecker J. Interaction of liposomal and polycationic transfection complexes with pulmonary surfactant. Journal of Gene Medicine 1999;1(5):331-340.

51. Plank C, Zauner W, Wagner E. Application of membrane-active peptides for drug and gene delivery across cellular membranes. Advanced Drug Delivery Reviews 1998;34(1):21-35.

52. Wyman TB, Nicol F, Zelphati O, Scaria PV, Plank C, Szoka FC. Design, synthesis, and characterization of a cationic peptide that binds to nucleic acids and permeabilizes bilayers. Biochemistry 1997;36(10):3008-3017.

53. Plank C, Mechtler K, Szoka FC, Wagner E. Activation of the complement system by synthetic DNA complexes: A potential barrier for intravenous gene delivery. Human Gene Therapy 1996;7(12):1437-1446.

54. Bogre L, Jonak C, Mink M, Meskiene I, Traas J, Ha DTC, Swoboda I, Plank C, Wagner E, HeberleBors E, Hirt H. Developmental and cell cycle regulation of alfalfa nucMs1, a plant homolog of the yeast Nsr1 and mammalian nucleolin. Plant Cell 1996;8(3):417-428.

55. Wyman TB, Plank C, Szoka FC. Reversible Attachment of Effectors to Plasmid DNA for Gene-Therapy. Abstracts of Papers of the American Chemical Society 1995;210:8-NUCL.

56. Wagner E, Buschle M, Mechtler K, Kichler A, Plank C, Zauner W, Blaas D, Kuchler E, Zatloukal K, Cotten M, Birnstiel ML. Receptor-Mediated Gene-Transfer and Endosomal Release. Journal of Cellular Biochemistry 1995:358-358.

57. Prchla E, Plank C, Wagner E, Blaas D, Fuchs R. Virus-Mediated Release of Endosomal Content in-Vitro - Different Behavior of Adenovirus and Rhinovirus Serotype-2. Journal of Cell Biology 1995;131(1):111-123.

58. Plank C, Oberhauser B, Mechtler K, Koch C, Wagner E. The Influence of Endosome-Disruptive Peptides on Gene-Transfer Using Synthetic Virus-Like Gene-Transfer Systems. Journal of Biological Chemistry 1994;269(17):12918-12924.

59. Cotten M, Wagner E, Zatloukal K, Buschle M, Chiocca S, Plank C, Zauner W, Schmidt W, Birnstiel ML. Receptor-Mediated Gene Delivery. Journal of Cellular Biochemistry 1994:214-214.

60. Zatloukal K, Wagner E, Cotten M, Schmidt W, Plank C, Berger M, Saltik M, Stingl G, Birnstiel ML. Receptor-Mediated Cytokine Gene Delivery to Tumor-Cells for Generation of Cancer Vaccines. Journal of Cellular Biochemistry 1993:129-129.

61. Wagner E, Cotten M, Zatloukal K, Plank C, Curiel DT, Stingl G, Birnstiel ML. Receptor-Mediated Gene Delivery and Its Augmentation by Endosome-Disruptive Viruses or Peptides. Journal of Cellular Biochemistry 1993:210-210.

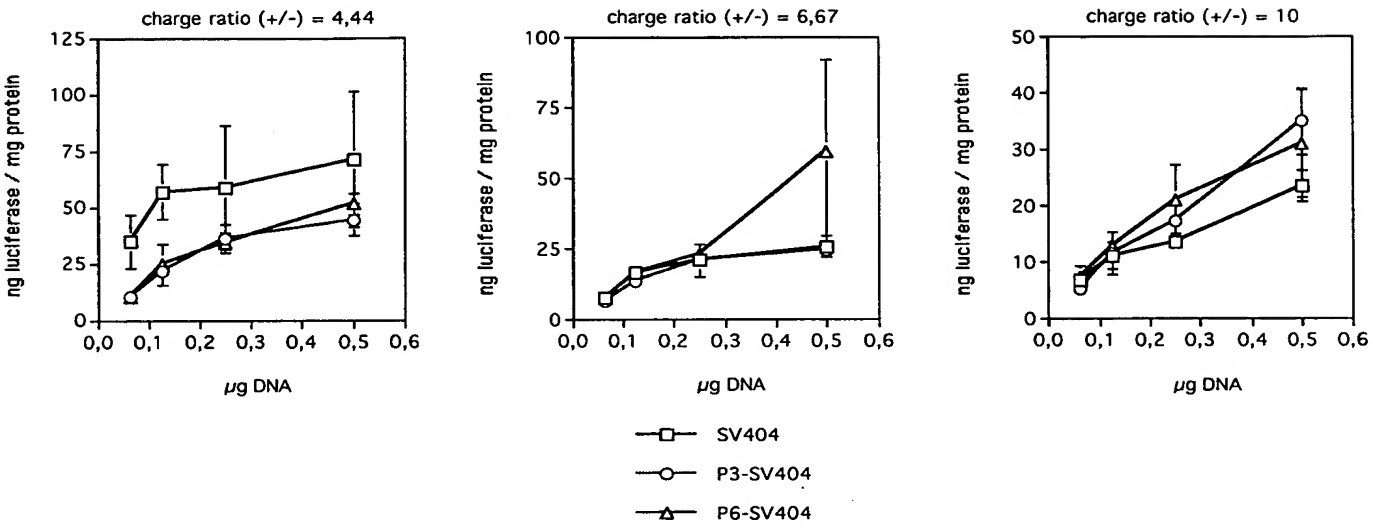
62. Briegel K, Lim KC, Plank C, Beug H, Engel JD, Zenke M. Ectopic Expression of a Conditional Gata-2 Estrogen-Receptor Chimera Arrests Erythroid-Differentiation in a Hormone-Dependent Manner. Genes & Development 1993;7(6):1097-1109.

63. Zatloukal K, Wagner E, Cotten M, Phillips S, Plank C, Steinlein P, Curiel DT, Birnstiel ML. Transferinfection - a Highly Efficient Way to Express Gene Constructs in Eukaryotic Cells. Annals of the New York Academy of Sciences 1992;660:136-153.

64. Wagner E, Plank C, Zatloukal K, Cotten M, Birnstiel ML. Influenza-Virus Hemagglutinin-Ha-2 N-Terminal Fusogenic Peptides Augment Gene-Transfer by Transferrin Polylysine DNA Complexes - toward a Synthetic Virus-Like Gene-Transfer Vehicle. Proceedings of the National Academy of Sciences of the United States of America 1992;89(17):7934-7938.

65. Plank C, Zatloukal K, Cotten M, Mechtler K, Wagner E. Gene-Transfer into Hepatocytes Using Asialoglycoprotein Receptor Mediated Endocytosis of DNA Complexed with an Artificial Tetra-Antennary Galactose Ligand. Bioconjugate Chemistry 1992;3(6):533-539.

Exhibit B



Luciferase reporter gene delivery to HeLa cells using the cationic copolymers P3-SV404 and P6-SV404 in comparison with the cationic peptide SV404 $(PKKKRKVG)_4C$ at different charge ratios. DNA complexes were formed together with the endosomolytic peptide INF7. The results demonstrate that the copolymers yield similar transfection efficiencies as the peptide SV404.